REMARKS

Reconsideration of the above-identified application in view of the amendments above and the remarks following is respectfully requested.

Claims 1-14 are in this case. Claims 9-14 were withdrawn under a restriction requirement as drawn to a non-elected invention. Claim 2 was previously cancelled. Claims 1-8 have been rejected. Claim 1 has now been amended.

35 U.S.C. § 102 Rejections

The Examiner has rejected claims 1 and 3-5 under 35 U.S.C. § 102(b) as being anticipated by Park *et al.* (Facial Plastic Surgery 11: 278-283, 1995).

The Examiner points out that Applicant had argued that Park *et al.* do not teach using 'template-free" cells and therefore do not anticipate the claimed invention. However, Applicant's claims only require that the cartilage producing cells are in suspension. The Examiner asserts that chondrocytes seeded into a template, as per Park *et al.* teaching, is considered a suspension of chondrocytes mixed with a solid.

In order to overcome the Examiner's rejection claim 1 has been amended to exclude a support or solid particles from the cell suspension of the claimed invention. Accordingly, amended claim 1 currently recites:

"A method of cosmetically repairing a skin contour irregularity in a subject, the method comprising introducing a support free suspension of cultured isolated cartilage-producing cells devoid of solid particles into the skin contour irregularity thereby effecting cosmetic repair thereof."

Support for this amendment can be found throughout the instant application. For example, the Examples section describes cultured isolated cartilage-producing cells suspended only in "...saline or any other physiologically acceptable buffer for injection" (page 17 lines 13-14), clearly, indicating that the suspension of the present invention comprises cells and physiologically acceptable buffer only. Furthermore, the present invention teaches that "A small volume of cell suspension injected into the site of the subcutaneous contour defect will eventually fill the defects. Contact inhibition will prevent over-filling of the defect so that depressions do not become

bumps" (page 12 lines 9-12). Such results cannot be achieved using cell suspensions which include support (e.g., template) or solid particles since they may interfere in the process of self filling of subcutaneous contour defects. Thus, it is clear from the teachings of the instant application that the suspension of cells of the present invention is devoid of a support and solid particles.

In view of the above amendment, Applicant believes to have overcome the 35 U.S.C. § 102(b) rejection over Park *et al.*

The Examiner has also rejected claims 1 and 3-5 under 35 U.S.C. § 102(b) as being anticipated by Kim *et al.* (Plastic and Reconstructive Surgery 94: 233-237, 1994).

The Examiner points out that Applicant had argued that Kim *et al.* do not teach using "isolated non-engineered cells" and therefore do not teach the claimed invention. However, Applicant's claims only require that cartilage producing cells are in suspension. The Examiner asserts that chondrocytes described by Kim *et al.* are used in a manner similar to that of Park *et al.* and thus Kim *et al.* anticipate the claimed invention for the same reasons as pointed out above for Park *et al.*

In order to overcome the Examiner's rejection claim 1 has been amended, as described hereinabove, to exclude a support and/or solid particles from the cells suspension of the claimed invention.

In view of the above amendment, Applicant believes to have overcome the 35 U.S.C. § 102(b) rejection over Kim *et al.*

35 U.S.C. § 103 Rejections

The Examiner has rejected claims 1 and 7 under 35 U.S.C. § 103(a) as being unpatentable over Park *et al.*

The Examiner points out (in the Office Action dated December 17, 2002) that Park *et al.* teach using chondrocyte implants in facial cosmetic procedures. The Examiner further points out that while Park *et al.* do not teach treating rhytids, subcutaneous defects or depression, these types of facial defects are well known irregularities which are treated using facial cosmetic procedures. The Examiner

therefore asserts that that a person of ordinary skill in the art would reasonably expect that the method of Park *et al.* could be used to treat these skin irregularities.

Applicant wishes to point out that Park *et al.* teach use of chondrocyte-seeded template, which is in sharp contrast to the support free suspension of cultured isolated cartilage-producing cells devoid of solid particles of the present invention.

The use of suspended cells provides many substantial advantages over cell-seeded template in treating cosmetic defects. For example, the use of template-free suspended cells requires a less invasive approach for implantation. In addition, qualities unique to isolated cartilage producing cells ensure that a filled contour irregularity is more capable of resisting facial muscles movements thus substantially reducing the chances of wrinkles or rhytids returning. Furthermore, since chondrocytes will only proliferate until contact inhibition, the use of a template-free chondrocytes suspension ensures that contour depressions do not become unsightly bumps.

Thus, clearly, the use of support-free suspended cultured isolated cartilage-producing cells devoid of solid particles, according to the teaching of the present invention, is distinct from, and advantageous over, the teaching Park *et al.* Since Park *et al.* do not describe or suggest using support-free suspended cultured isolated cartilage-producing cells devoid of solid particles, an ordinary skilled artisan would not be motivated by Park *et al.* to practice the present claimed invention.

The Examiner has also rejected claims 1 and 4-7 under 35 U.S.C. § 103(a) as being unpatentable over Kim *et al.* for essentially the same reasons as stated above. The Examiner points out that since Kim *et al.* teach using cartilage harvested from a different species than a subject (xenogeneic source) without producing adverse effects, it should therefore be obvious that cartilage could harvested from the subject, a syngeneic source or an allogeneic source.

Applicant wishes to point out that, like Park *et al.*, Kim *et al.* teach implanting a chondrocytes-seeded template, which is in sharp contrast to the support-free suspension of cultured isolated cartilage-producing cells devoid of solid particles, utilized by the present invention. Since Kim *et al.* do not describe or suggest using support-free suspended cultured isolated cartilage-producing cells, nor

do they expound on the advantages of using such preparations, an ordinary skilled artisan would not be motivated by Kim *et al.* to practice the method of the claimed invention.

The Examiner has rejected claims 1 and 3-8 under 35 U.S.C. § 103(a) as being unpatentable over U.S. Pat. No. 4,469,676 in view of Atala *et al.* (J. Urol. 150: 745-747, 1993).

The Examiner points out that U.S. Pat. No. 4,469,676 teaches a method of treating wrinkles by injecting cartilage cells into the wrinkle. However, it does not teach using isolated cartilage producing cells to treat wrinkles. The Examiner also points out that Atala *et al.* teach that chondrocytes can be administered via subcutaneous injection for use in plastic and reconstructive surgery (see page 747, last paragraph). The Examiner further points out that the function of Atala *et al.* is to introduce cartilage at the injection site. Thus, the Examiner asserts that Atala *et al.* show that it was known in the art that isolated chondrocytes can be used for the same purpose as the cartilage of U.S. Pat. No. 4,469,676 and therefore, a person of ordinary skill in the art would have been motivated to treat wrinkles by subcutaneously injecting chondrocytes into the site of the wrinkle.

In addition, the Examiner points out that Atala *et al.* teach isolating chondrocytes from a calf and injecting the chondrocytes to a mouse. The Examiner asserts that if cells from a xenogenic source do not produce adverse effects, it is reasonable to expect that cells from the subject, a syngeneic source or an allogeneic source would also not produce adverse effects while still imparting the same benefit to the skin. The Examiner therefore concludes that a person of ordinary skill in the art would be motivated to use chondrocyte cells from the subject, a syngeneic source or an allogeneic source in the skin treatment method taught by the combined teaching of Atala *et al.* and U.S. Pat. No. 4,469,676.

Applicant wishes to point out that the Examiner is incorrect in asserting that Atala *et al.* teach that isolated chondrocytes can be administered via subcutaneous injection for use in plastic and reconstructive surgery. In fact, Atala *et al.* teach using an injectable biodegradable polymer (alginate) embedded with chondrocytes. The chondrocytes-embedded alginate "...serve as a synthetic support for injectable

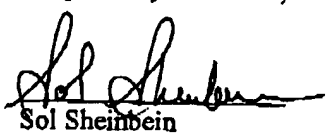
delivery and maintenance of cartilage architecture *in vivo*." (page 745, last paragraph of the introduction). According to the teaching of Atala *et al.*, the new cartilage produced by the chondrocytes-embedded alginate "...retains the approximate configuration and dimensions of the injected template" (page 747. 3rd paragraph). The containment of the formed cartilage within the alginate template is advantageous for the purpose of treating vesicoureteral reflux or similar conditions. However, chondrocytes-embedded alginate is impractical for use in treating skin contour irregularities since it does not allow filling of contour defects by proliferating chondrocytes, or in turn, may result in over-filling problems. In sharp contrast, the present invention teaches injecting a support-free suspension of cartilage-producing cells devoid of solid particles into the site of the subcutaneous contour defect which will eventually fill the defect. Contact inhibition will prevent over-filling of the defect so that depressions do not become bumps (see page 12 lines 7-12 of the instant application).

Applicant further wishes to point out that Atala *et al.* teach using chondrocytes-embedded alginate for treating vesicoureteral reflux by forming a cartilage capable of effectively blocking the reflux (backward flow of urine from the bladder back into ureter). For this purpose a polymer support is essential in order to support the formation of a properly positioned rigid cartilage. Accordingly, the reference states that "We have also shown that the cell-polymer construct is essential in that the injection of free chondrocytes or alginate alone does not result in cartilage formation" (page 747 3rd paragraph), thereby explicitly teaching against the present invention.

Hence, clearly, a person of ordinary skill in the art could not have been motivated to treat skin contour irregularities with a suspension of cultured isolated cartilage-producing cells, by the teaching of Atala *et al.* or by the combined teaching of Atala *et al.* and U.S. Pat. No. 4,469,676.

In view of the above amendments and remarks it is respectfully submitted that claims 1 and 3-8 are now in condition for allowance. Prompt notice of allowance is respectfully and earnestly solicited.

Respectfully submitted,



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